REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 60 is currently being amended to delete "derivatives". No new matter is added.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 57-68 are now pending in this application.

The present case has been finally rejected. Entry of this amendment is respectfully requested as it merely limits the claims to overcome the rejection under 35 U.S.C. § 112, first paragraph and better place the application in condition for allowance. No new search is required, and consideration of the arguments is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 60-61 were rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. Specifically, the Examiner asserts that the term "furan derivatives" encompasses a broad genus of compounds. Without acquiescing to this rejection and solely to expedite prosecution, "derivatives" has been deleted in claim 60, which now recites "furan". As furan is a well known compound and does not encompass a broad genus as alleged by the Examiner, Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 47-63, 66 and 68 were rejected under 35 U.S.C. § 102(a) for allegedly being anticipated by Maheu (*Arthritis & Rheumatism* (1998) 41:81-91). As the Examiner notes "Maheu teaches a clinical trial of avocado/soybean unsaponifiables (ASU) in the treatment of patients with symptomatic *osteoarthritis* of the knee or hip." (Office Action, page 3, emphasis added, citation omitted). Maheu does not teach the treatment of osteoporosis. Applicants respectfully traverse this rejection.

An anticipation rejection under 35 U.S.C. § 102 requires a showing that each limitation of a claim is found in a single reference, practice or device. *See In re Donohue*, 766 F.2d 531 (Fed. Cir. 1985). In order for a reference to be anticipatory, it must "be enabling and describe the applicant's claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention." *See In re Paulsen*, 30 F.3d 1475 (Fed. Cir. 1994). Applicants assert that the cited references do not anticipate the present claims as they do not teach each and every element of the claims.

Osteoarthritis and osteoporosis are very different disorders that attack different tissues, have different origins, and are treated differently. Osteoarthritis is an immune-related condition characterized by the progressive destruction of *articular cartilage*, as well as by synovium and tendon inflammation, muscle weakness, osteophyte formation and subchondral bone plate thickening. In contrast, osteoporosis is a disease of *bone* that leads to bone skeletal fragility and an increased risk and/or incidence of fracture. In osteoporosis the bone mineral density (BMD) is reduced, bone microarchitecture is disrupted, and the amount and variety of non-collagenous proteins in bone is altered.

During osteoporosis, the loss of bone is due to increased osteoclastic activity leading to bone resorption, and bone resorption is superior to bone formation. Bone resorption in osteoarthritis is significantly lower than for osteoporosis, and bone density is greater in patients with osteoarthritis as compared to osteoporosis. For instance, Dequeker (Dequeker J, Aerssens J, Luyten FP, *Aging Clin Exp. Res.* (2003); 15:426-39, abstract provided as Exhibit A) teaches that:

- the anthropometric differences of patients suffering from osteoarthritis compared with osteoporosis are well established. Osteoarthritis cases have stronger body build and are more obese,

- with aging, the bone loss in osteoarthritis is lower, except when measured near an affected joint (hand, hip, and knee). The lower degree of bone loss with aging is explained by lower bone turnover as measured by bone resorption-formation parameters. Osteoarthritis cases not only have higher apparent and real bone density, but also wider geometrical measures of the skeleton, diameters of long bones and trabeculae, both contributing positively to better strength and fewer fragility fractures,

- these general bone characteristics of osteoarthritis bone may explain the inverse relationship osteoarthritis- osteoporosis and why osteoarthritis cases have fewer fragility fractures,

- instead, the osteoblast regenerative capacity of bone in osteoporosis is compromised compared with osteoarthritis.

Further, Stewart ((Stewart *et al, J. Rheumatol.* (1999), 26:622-6, abstract provided as Exhibit B) teaches that:

- osteoarthritis and osteoporosis are reported to be rare in the same patient,

- there were differences in bone density, the patients with osteoporosis having lower bone density, while patients with osteoarthritis had similar or increased bone density compared to controls,

- increased bone turnover was restricted to the osteoarthritis group.

The Examiner considers that the teaching of Maheu *inherently* includes the treatment of individuals with osteoporosis, alleging that according to his statistical calculations, 3 women in the Maheu study would have both osteoarthritis and osteoporosis. However, as noted above, Dequeker and Stewart indicate that these two conditions rarely occur in the same patient since osteoarthritic patients typically had a stronger bone density, and thus, the Examiner's reliance on combining the prevalence of the disorders in the general population is not supported by the facts.

Further, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. *Inherency, however, may not be established by probabilities or possibilities.* The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted, emphasis added). Thus, the Examiner improperly relies upon (misapplied) statistics based on the prevalence of the diseases in the general population to establish inherency.

Because the Examiner cannot rely on Maheu to inherently disclose the treatment of osteoporosis for both scientific and legal reasons, it cannot anticipate the claimed invention. Therefore, Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 57, 64-65 and 67 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Maheu and Rancurel (U.S. Pat. No. 5,498,411). Applicants respectfully traverse this rejection.

The Supreme Court has recently reaffirmed the *Graham* factors for the determination of obviousness. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727,1739 (2007) 127 S. Ct. 1727 (2007) (holding that the proper inquiry for determining obviousness is whether the improvement is more than the predictable use of prior art elements according to their established functions). These four factual inquiries under *Graham* are: 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the prior art and the claims in issue; 3) resolving the level of ordinary skill in the prior art; and 4) evaluating evidence of secondary consideration. *Graham v. John Deere*, 383 U.S. 17-18 (1966). In accordance with these factors, to establish a *prima facie* obviousness of the claimed

invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). Applicants assert that this burden has not been met.

The Examiner applies Maheu as described above, namely that it teaches the treatment of osteoporosis with ASU. Rancurel is applied as teaching the preparation of nonsaponifiable matter of avocado oil and extracts of soya bean oil for use in pharmaceuticals and food additives. However, Rancurel expressly notes that this matter is useful for connective tissue disorders (such as cartilage health) as well as a comfort to the elderly. Rancurel, col. 1, lines 31-37 and col. 2, lines 48-52. At no point does Rancurel mention the use of its compositions for the treatment of osteoporosis. As stated before, osteoporosis affects the bone based on the activity of osteoblasts. Rancurel and Maheu both teach treating different targets, namely the connective tissue and cartilage, and Maheu in particular teaches treating a disorder, osteoarthritis, that is known to be associated with a greater bone density than osteoporosis. A person of skill in the art would recognize these critical differences and therefore would not apply the teachings of the cited art to use unsaponifiable components of avocado oil and soya bean oil treat osteoporosis. Because the cited art, alone or in combination, fail to teach each and every limitation of the claims, it cannot render the present claims obvious. Applicants therefore respectfully request that the rejection be withdrawn.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to

charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date: April 7, 2008

By: _____

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Exhibit A

ABSTRACTS

Dequeker J, Aerssens J, Luyten FP.
Aging Clin Exp Res. 2003 Oct;15(5):426-39.

Osteoarthritis and osteoporosis: clinical and research evidence of inverse relationship.

The etiology of osteoporosis (OP) and osteoarthritis (OA) is multifactorial: both constitutional and environmental factors, ranging from genetic susceptibility, endocrine and metabolic status, to mechanical and traumatic injury, are thought to be involved. When interpreting research data, one must bear in mind that pathophysiologic factors, especially in disorders associated with aging, must be regarded as either primary or secondary. Therefore, findings in end-stage pathology are not necessarily the evidence or explanation of the primary cause or event in the diseased tissue. Both aspects of research are important for potentially curative or preventive measures. These considerations, in the case of our topic--the inverse relationship of OP and OA--are of particular importance. Although the inverse relationship between two frequent diseases associated with aging, OA and OP, has been observed and studied for more than 30 years, the topic remains controversial for some and stimulating for many. The anthropometric differences of patients suffering from OA compared with OP are well established. OA cases have stronger body build and are more obese. There is overwhelming evidence that OA cases have increased BMD or BMC at all sites. This increased BMD is related to high peak bone mass, as shown in mother-daughter and twin studies. With aging, the bone loss in OA is lower, except when measured near an affected joint (hand, hip, knee). The lower degree of bone loss with aging is explained by lower bone turnover as measured by bone resorption-formation parameters. OA cases not only have higher apparent and real bone density, but also wider geometrical measures of the skeleton, diameters of long bones and trabeculae, both contributing positively to better strength and fewer fragility fractures. Not only is bone quantity in OA different but also bone quality, compared with controls and OP cases, with increased content of growth factors such as IGF and TGFbeta, factors required for bone repair. Furthermore, in vitro studies of osteoblasts recruited from OA bone have different differentiation patterns and phenotypes. These general bone characteristics of OA bone may explain the inverse relationship OA-OP and why OA cases have fewer fragility fractures. The role of bone, in particular subchondral bone, in

the pathophysiology, initiation and progression of OA is not fully elucidated and is still controversial. In 1970, it was hypothesized that an increased number of microfractures lead to an increase in subchondral bone stiffness, which impairs its ability to act as a shock absorber, so that cartilage suffers more. Although subchondral bone is slightly hypomineralized because of local increased turnover, the increase in trabecular number and volume compensates for this, resulting in a stiffer structure. There is also some experimental evidence that osteoblasts themselves release factors such as metalloproteinases directly or indirectly from the matrix, which predispose cartilage to deterioration. Instead, the osteoblast regenerative capacity of bone in OP is compromised compared with OA, as suggested by early cell adhesion differences. The proposition that drugs which suppress bone turnover in OP, such as bisphosphonates, may be beneficial for OA is speculative. Although bone turnover in the subchondral region of established OA is increased, the general bone turnover is reduced. Further reduction of bone turnover, however, may lead to overmineralized (aged) osteons and loss of bone quality, resulting in increased fragility.

Exhibit B

Stewart A, Black A, Robins SP, Reid DM.

J Rheumatol. 1999 Mar;26(3):622-6.

Bone density and bone turnover in patients with osteoarthritis and osteoporosis.

OBJECTIVE: Osteoarthritis (OA) and osteoporosis (OP) are reported to be rare in the same patient. We examined bone mass, bone turnover, and radiological presence of OA in a group of patients with OA with previous hip fractures and age matched controls. METHODS: Bone mass was assessed by bone mineral density (BMD), using dual energy x-ray absorptiometry (DEXA) of the hip and total body, and quantitative ultrasound of the os calcis, measuring broadband ultrasound attenuation and velocity of sound. Bone turnover was assessed by measuring urinary pyridinium crosslinks and serum osteocalcin. RESULTS: There were differences in bone density, the patients with OP having lower bone density, while patients with OA had similar or increased bone density compared to controls, Serum osteocalcin showed no significant differences among the 3 groups of patients. Urinary pyridinium crosslinks excretion was significantly elevated in the OA group but not in the OP group compared with controls. CONCLUSION: Increased bone turnover was restricted to the OA group.